Remarks

Upon entry of the foregoing amendment, claims 1, 3-5, 7-13, 16 and 20 are pending in the application, with claim 1 being the sole independent claim. Claims 2, 6, 14, 15, 17, 18, 19, 21 and 22 are canceled without prejudice or disclaimer of the subject matter therein. These changes are believed to introduce no new matter, and their entry is respectfully requested.

The amendments to claims 1 and 3 are directed to different embodiments of the present invention and are intended and to put the claims in condition for allowance.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

I. Rejections Under 35 U.S.C. § 112, First Paragraph

A. Written Description / New Matter

The Examiner has rejected claims 1-5, 7-13, 15-17, 19 and 20 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement (new matter). The Examiner asserts that there is no support for

> culture media that consist of DMEM (Dulbecco's modified Eagle's medium), F12 medium, insulin and one or more additives selected from the group consisting of NaHCO3, sugars, ethanolamine, pyruvate, amino acids and mixtures thereof.

(OA at page 3.)

Applicants respectfully disagree with the Examiner's position. However, solely in an effort to advance prosecution, and not in acquiescence to any reasoning underlying

the Examiner's rejection, claim 1 has been amended to specifically recite the sugars and amino acids added as the supplement to the DMEM and F12 media. As such, Applicants respectfully submit that the rejection has been rendered moot and request its withdrawal.

B. Enablement

The Examiner has rejected claims 1-5, 7-13, 15-17, and 19-22 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. More specifically, the Examiner asserts that "[i]n the instant case large scale industrial production of rEPO in SF conditions (as claimed) is not considered to routine in the art and without sufficient guidance to the host cells, contents and concentrations in the culture media used the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue." (OA at page 8.) Applicants respectfully traverse this rejection, and request that the Examiner reconsider and withdraw the rejection in view of the remarks below.

Contrary to the Examiner's assertions, a person of ordinary skill in the art could practice the present invention without undue experimentation, based on the guidance in the specification and the level of skill in the art. Undue experimentation does not mean "no" experimentation, only that it be reasonable. *See, e.g., In re Wands*, 858 F.2d at 737 ("The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed."). In contrast to the Examiner's assertion, it is clear from the combination of references cited by the Examiner that the state of the art is such

that recombinant proteins can be successfully produced in cells grown in SF media without undue experimentation.

The references cited by the Examiner teach a variety of SF media to produce rEPO from the cells in culture. The Tang *et al.*, Schroeder *et al.* and Wang *et al.* references cited by the Examiner teach that the ordinary artisan can adapt a cell line to grow in SF medium and achieve production of the recombinant protein. For example, removal of protein components such as "fetuin and coating of the tissue culture dishes with 5 $\mu g/cm^2$ fibronectin did not interfere with the growth of any cell line." (*See* Schroeder *et al.*, 3.8 Protein-Free Medium Formulation, page 288.) In addition, "[o]nly minor changes in the medium formulation were necessary for its use in the cultivation of anchorage-dependent and suspension cells. Adaptation of cells grown in the SF formulation to a protein free medium was easy and straight forward." (*See* Schroeder *et al.*, 4. Conclusion, page 290.) As such, Schroeder *et al.* clearly teach that optimizing a media formulation to grow cells in SF medium is well within the skill of the ordinary artisan and would not require undue experimentation. The teaching in the art in conjunction with the Example provided in the specification indicate that a person of ordinary skill in the art at the time of filing would have possessed the knowledge and skills necessary to make and test the compositions of the present invention. Thus, any experimentation required to practice the present invention would have been reasonable, not undue.

The Examiner has cited *Fields v. Conover*, 433 F.2d 1386 (CCPA 1970) for the holding that "[e]xperimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." (OA at page 7.) Here, the presently amended claim 1

provides a specific list of cell lines for the production of rEPO and additionally provides a list of specific additives for the DMEM and F12 medium for the production of rEPO from these cell lines. Thus, the only thing remaining for the ordinary artisan is determining the concentration of additives. Determining the concentration of additives for a medium for the production of a recombinant protein by culture can easily be achieved by statistical optimizations based on the Placket-Burman design, for example. *See* Lee *et al.*, "Development of a serum free medium for the production of erythropoietin by suspension culture of recombinant Chinese hamster ovary cells using a statistical design," *J. Biotech.*, 69:85-93 (1999) cited on the IDS submitted April 21, 2005. Additionally, in the Schroeder *et al.* reference previously cited by the Examiner, the production of a protein free medium is achieved by the removal or addition of individual components followed by observing the growth of the cells. As pointed out by Schroeder *et al.* and Lee *et al.*, these optimization techniques would not require ingenuity beyond those of the ordinary laboratory worker, especially when the laboratory worker is already given the specific additives to include in the medium.

In summary, Applicants assert that present claims 1, 3, 4, 5, 7-13, 16 and 20 are fully enabled by the specification. Therefore, Applicants respectfully request reconsideration and withdrawal of this rejection.

II. Rejection Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 1-5, 7-13, 15-17, 19 and 20 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regards as the invention. (OA at

page 8.) More specifically, the Examiner asserts the claims are indefinite because they contain a "broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation." (OA at page 9.)

Applicants respectfully disagree with the application of this rejection. However, solely to advance prosecution, and not in acquiesce of any of the Examiner's assertions, claim 1 has been amended to read "wherein said culture medium consists of : (i) DMEM (Dulbecco's modified Eagle's medium); (ii) F12 medium; (iii) insulin; and (iv) $NaHCO_3$, glucose, lactose, galactose, ethanolamine, pyruvate, glutamine, tryptophan, asparagine, and serine as additives." The amendment has not changed the scope of the claim and solely has been made to more clearly define the invention. Reconsideration and withdrawal of this rejection is respectfully requested.

III. Double Patenting

The Examiner rejected claims 1-5, 7-13, 15-17, 19 and 20 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 7-13 of U.S. Patent No. 6,777,205, for the same reasons of record as set forth in the Office Action mailed 12/29/05. (OA at page 10.) Applicants respectfully disagree with the Examiner's assertion. However, solely to advance prosecution, Applicants will submit a terminal disclaimer in accordance with 37 C.F.R. § 1.321(c) upon the notification by the Examiner of allowable subject matter.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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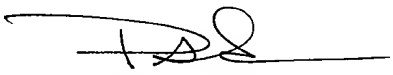

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